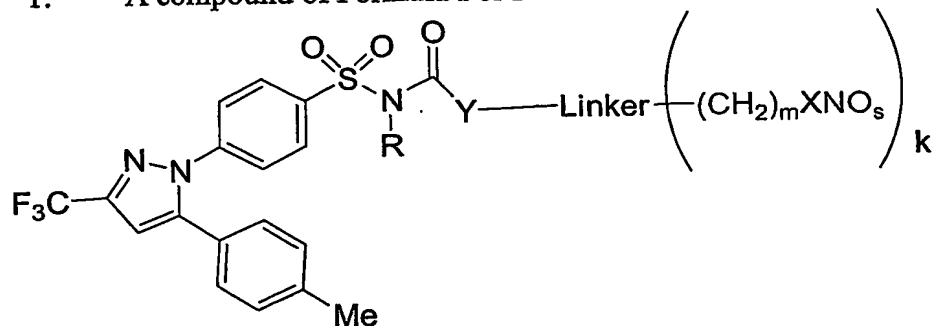
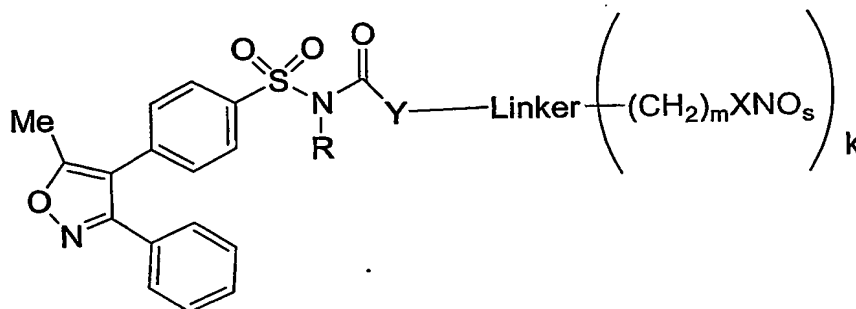


WHAT IS CLAIMED IS:

1. A compound of Formula I or Formula II



Formula I



Formula II

or a pharmaceutically acceptable salt thereof wherein

each s is independently 1 or 2;

15 k is 1, 2, 3 or 4;

each m is independently 0, 1, 2, 3 or 4;

each X is independently O or S;

Y is a bond, S, O or NR_1 , wherein R_1 is hydrogen or C_{1-6} alkyl;

R is hydrogen or C_{1-6} alkyl;

20 the Linker is selected from the group consisting of:

- (a) $-(CH_2)_n$, wherein n is 0, 1, 2, 3 or 4,

- (b) C₃₋₆cycloalkyl, wherein the C₃₋₆cycloalkyl optionally mono-, di- or tri-substituted with a substituent selected from the group consisting of (1) halo,
(2) C₁₋₃alkyl,
(3) C₁₋₃alkoxy,
5 (4) Hydroxy,
(5) NO₂,
(6) CO₂,
(7) CF₃,
(8) CN;
10 (9) CH₂COOH
(10) CH₂COO-C₁₋₃alkyl,
(11) C₁₋₃alkthio,
- (c) aryl, wherein the aryl is selected from the group consisting of phenyl and naphthyl, wherein the aryl is optionally mono-, di- or tri-substituted with a
15 substituent selected from the group consisting of
(1) halo,
(2) C₁₋₃alkyl,
(3) C₁₋₃alkoxy,
(4) Hydroxy,
20 (5) NO₂,
(6) CO₂,
(7) CF₃,
(8) CN;
(9) CH₂COOH
25 (10) CH₂COO-C₁₋₃alkyl,
(11) C₁₋₃alkthio,
- (d) Heteroaryl optionally mono-, di- or tri- substituted with substituents selected from the group consisting of,
30 (1) halo,
(2) C₁₋₃alkyl,
(3) C₁₋₃alkoxy,
(4) Hydroxy,
(5) NO₂,
(6) CO₂,

- (7) CF₃,
(8) CN;
(9) CH₂COOH
(10) CH₂COO-C₁₋₃alkyl,
(11) C₁₋₃alkthio.

2. The compound according to Claim 1 wherein

s is 2;
k is 1;
m is 1 or 2.

3. The compound according to Claim 1 wherein

X is O;
R is H.

4. The compound according to Claim 1 wherein

R is H; and
Y is a bond.

5. The compound according to Claim 1 wherein

R is H;
Y is a bond;
s is 2;
k is 1;
m is 1.

6. The compound according to Claim 2 wherein:
the Linker is -(CH₂)_n, wherein n is 1 or 2.

7. The compound according to Claim 2 wherein:
the Linker is C₃₋₆cycloalkyl, wherein the C₃₋₆cycloalkyl optionally mono-, di- or tri-substituted
with a substituent selected from the group consisting of

- (1) halo,
(2) Methyl,

- (3) Methoxy,
(4) Hydroxy,
(5) NO₂,
(6) CO₂,
5 (7) CF₃,
(8) CN, and
(9) CH₂COOH.

8. The compound according to Claim 2 wherein:
10 the Linker is aryl, wherein the aryl is selected from the group consisting of phenyl and naphthyl, wherein the aryl is optionally mono-, di- or tri-substituted with a substituent selected from the group consisting of

- (1) halo,
(2) Methyl,
15 (3) Methoxy,
(4) Hydroxy,
(5) NO₂,
(6) CO₂,
(7) CF₃,
20 (8) CN, and
(9) CH₂COOH.

9. The compound according to Claim 2 wherein:
25 the Linker is phenyl optionally mono-, di- or tri-substituted with a substituent selected from the group consisting of:

- (1) halo,
(2) Methyl,
(3) Methoxy,
(4) Hydroxy,
30 (5) NO₂,
(6) CO₂,
(7) CF₃,
(8) CN, and
(9) CH₂COOH.

10. The compound according to Claim 2 wherein:

the Linker is benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl,
benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolyl, furanyl,
imidazolyl, indolyl, indolyl, indolaziny, indazolyl, isobenzofuranyl, isoindolyl,
isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl,
pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl,
quinazolyl, quinolyl, quinoxalyl, thiadiazolyl, thiazolyl, thienyl, triazolyl,
azetidyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl,
pyrrolidinyl, morpholyl, thiomorpholyl, dihydrobenzimidazolyl,
dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl,
dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl,
dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl,
dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl,
dihydroquinolyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl,
dihydrothienyl, dihydrotriazolyl, dihydroazetidyl, methylenedioxybenzoyl,
tetrahydrofuranyl, and tetrahydrothienyl, optionally mono-, di- or tri- substituted
with substituents selected from the group consisting of,

- (1) halo,
- (2) Methyl,
- (3) Methoxy,
- (4) Hydroxy,
- (5) NO₂,
- (6) CO₂,
- (7) CF₃,
- (8) CN, and
- (9) CH₂COOH.

11. The compound according to Claim 10 wherein the Linker is selected from
pyridyl, each optionally mono-, di- or tri- substituted with substituents selected
from the group consisting of,

- (1) halo,
- (2) Methyl,

- (3) Methoxy,
(4) Hydroxy,
(5) NO₂,
(6) CO₂,
5 (7) CF₃,
(8) CN, and
(9) CH₂COOH.

12. The compound according to Claim 1 wherein s is 2.

10 13. A method of treating an inflammatory disease susceptible to treatment with a non-steroidal anti-inflammatory agent comprising administering to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound according to Claim 1.

15 14. The method according to Claim 13 wherein the patient is also at risk of a thrombotic cardiovascular event.

20 15. A method of treating cyclooxygenase mediated diseases advantageously treated by an active agent that selectively inhibits COX-2 in preference to COX-1 comprising administering to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound according to Claim 1.

25 16. The method according to Claim 15 wherein the patient is also at risk of a thrombotic cardiovascular event.

30 17. A method for treating a chronic cyclooxygenase-2 mediated disease or condition and reducing the risk of a thrombotic cardiovascular event in a human patient in need of such treatment and at risk of a thrombotic cardiovascular event comprising orally concomitantly or sequentially administering to said patient a compound according to Claim 1 in an amount effective to treat the cyclooxygenase-2 mediated disease or condition and aspirin in an amount effective to reduce the risk of the thrombotic cardiovascular event.

18. The method according to Claim 17 wherein the compound is administered orally on a once daily basis.

5 19. The method according to Claim 17 wherein the compound is administered orally on a twice daily basis.

10 20. The method according to Claim 17 wherein the cyclooxygenase-2 selective mediated disease or condition is selected from the group consisting of: osteoarthritis, rheumatoid arthritis and chronic pain.

21. The method according to Claim 17 wherein aspirin is administered at a dose of about 30 mg to about 1 g.

15 22. The method according to Claim 17 wherein aspirin is administered at a dose of about 80 to about 650 mg.

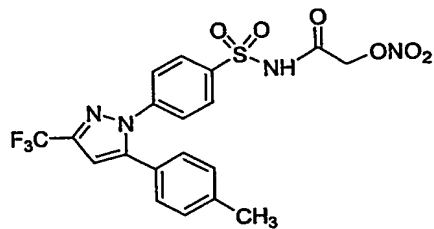
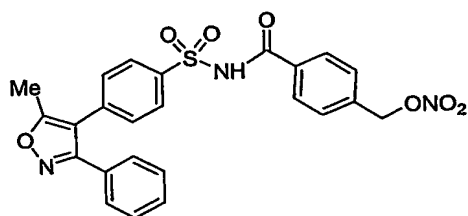
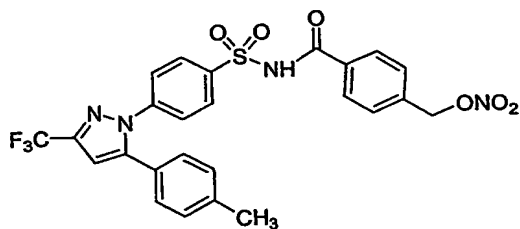
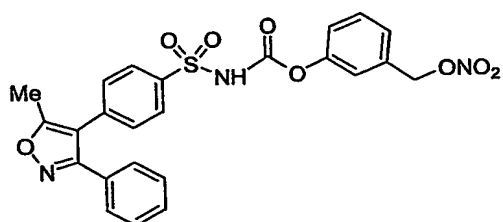
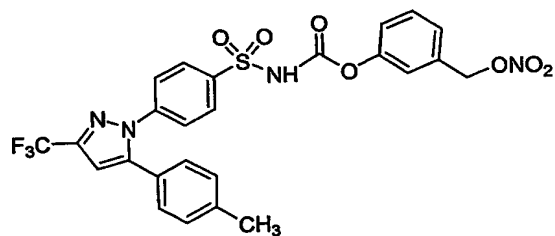
23. The method according to Claim 22 wherein aspirin is administered at a dose of about 81 mg or about 325 mg.

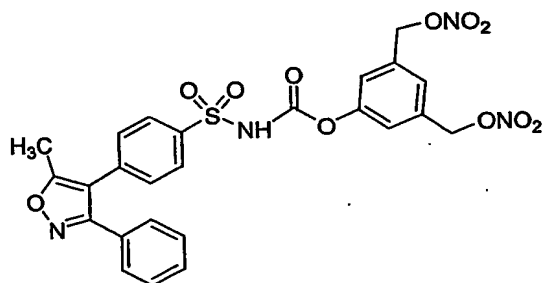
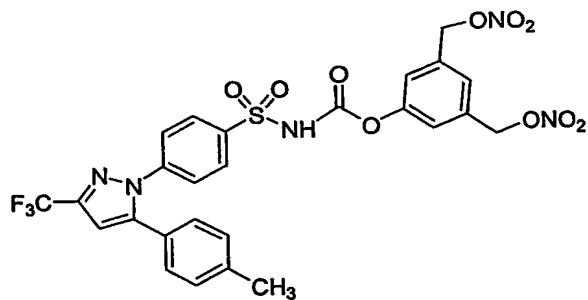
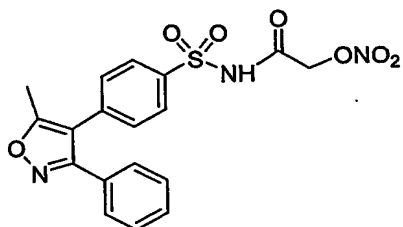
20 24. The method according to Claim 22 wherein aspirin is orally administered once daily.

25 25. A pharmaceutical composition comprising a compound according to any one of Claims 1 to 12 and aspirin in combination with a pharmaceutically acceptable carrier.

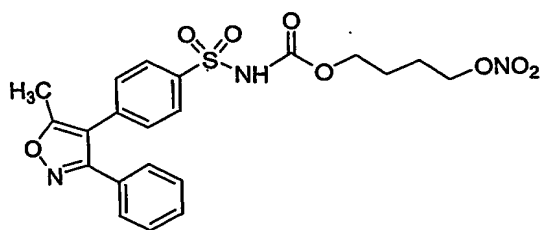
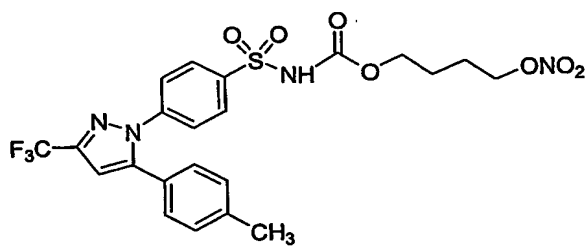
26. A pharmaceutical composition comprising a compound according to any one of Claims 1 to 12 and a pharmaceutically acceptable carrier.

27. A compound selected from the following group:



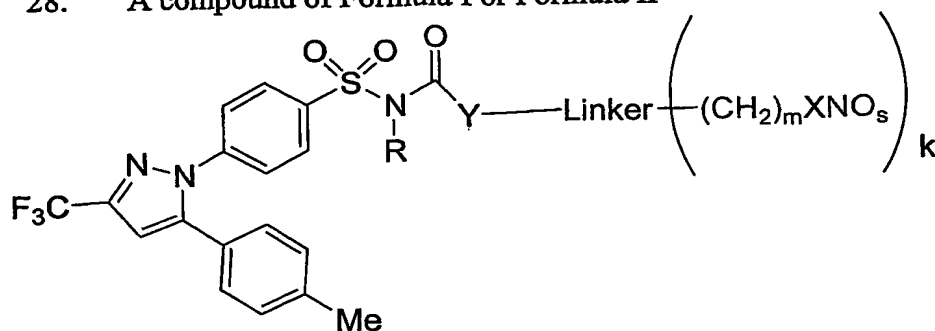


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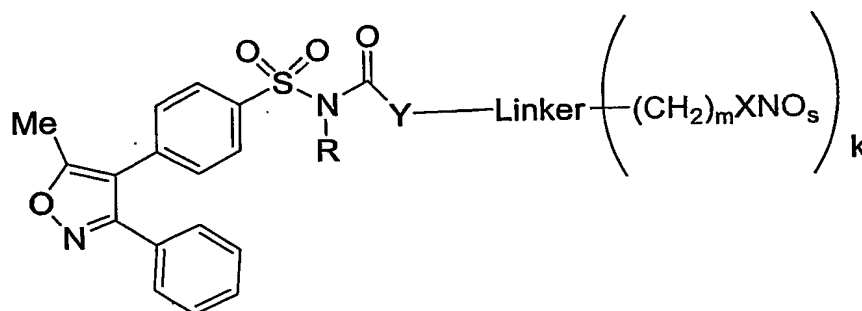


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28. A compound of Formula I or Formula II



Formula I



Formula II

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or a pharmaceutically acceptable salt thereof wherein
each s is independently 1 or 2;

10 k is 1, 2, 3 or 4;

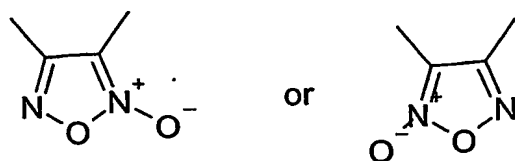
each m is independently 0, 1, 2, 3 or 4;

each X is independently O or S;

Y is a bond, S, O or NR₁, wherein R₁ is hydrogen or C₁-6alkyl;

R is hydrogen or C₁-6alkyl;

15 the Linker is selected from the group consisting of:



29. Use of a compound of any one of Claims 1 to 12, 27 or 28, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating an inflammatory disease.

30. A compound of any one of Claims 1 to 12, 27 or 28, or a pharmaceutically acceptable salt thereof, for use in medicinal therapy.

31. A compound of any one of Claims 1 to 12, 27 or 28, or a pharmaceutically acceptable salt thereof, for use in treating cyclooxygenase mediated diseases advantageously treated by an agent that selectively inhibits COX-2 in preference to COX-1.